REMARKS

Claims 1-14, 24-26, 28-30, 46-52, and 55-65 are pending and appear in this application for the Examiner's review and consideration. Of these claims, claims 6-14 and 55-65 are withdrawn from consideration based on a restriction requirement. Claims 2-6, 10, 28-29, 46, 50, 55, 57, and 61 are currently amended, and claim 27 is cancelled. Claim 2 is amended to further distinguish the claim from the cited art, and claims 46, 50, 55, and 57 are amended for clarity. Other claims such as claims 3-6, 10, 29 and 61, are amended to be consistent with the amendments to claim 2. Claims 46 and 55 are also amended to depend from claims 1 and 2, respectively. Claim 28 is amended to correct dependency. As no new matter is introduced, entry of the amendments at this time is warranted.

Applicants acknowledge with appreciation that claim 1 is in condition for allowance. Claim 46 is amended such that claims 46-52, 57-60 and 62-65 depend from claim 1, directly or indirectly. As such, claims 57-60 and 62-65 should be rejoined, and claims 46-52, 57-60 and 62-65 should be allowed since they incorporate the patentable features of claim 1 as well as include additional patentable features.

Claims 6-14, 55-56 and 61 are withdrawn from consideration as being drawn to a non-elected invention. However, these claims depend from claim 2, directly or indirectly, and therefore should be rejoined for examination and allowed when claim 2 is allowed.

Claims 46 and 52 are objected to because of informality. The objection to claim 46 is moot in view of the amendment to claim 46. The reference to claim 52 is believed to be an error, since claim 52 does not include the grammatically incorrect phrase identified by the Examiner. None of the other claims containing a similar recitation has this informality. Thus, this objection should be withdrawn.

Claims 2-5, 24-30, and 46-52 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement for the reasons set forth on pages 5-6 of the Office Action.

In particular, the Examiner states that the recitation of "replication-deficient NDV" in claims 2, 46 and 50 and the claims depending therefrom is not supported by the specification as originally filed. Applicants respectfully disagree.

The restricted ability of lentogenic NDV to replicate efficiently in culture, as well as in various tissues or organs, is well known in the art. In fact, as known in the art, this restricted ability is a property which distinguishes the lentogenic NDV from the velogenic and mesogenic NDV. For example, velogenic and mesogenic strains are cytopathic and produce plaques whereas lentogenic strains are sometimes cytopathic but appear to be unable to produce plaques in chicken embryo fibroblast and in Hela cells (*see* Diseases of Poultry, Fifth Edition, p. 640, (H.E. Biester and L.H. Schwarte, editors, Iowa State University Press, 1965). U.S. Patent No. 5,989,805 discloses that replication in cell cultures is restricted to velogenic and mesogenic strains of NDV, and that lentogenic NDV can replicate only in the presence of Mg^{2+} and DEAE or in the presence of trypsin. U.S. Patent No. 6,719,979 also discloses that lentogenic NDV can replicate efficiently only in the intestinal and respiratory tract, while the other pathogenic NDV strains, namely, mesogenic and velogenic strains, can replicate efficiently in various tissues and organs without such limitation. It is also known that lentogenic strains of NDV are unable to propagate in the MDBK cell line, in contrast to mesogenic and velogenic strains which can propagate efficiently in such cells (*see* King D. J. (Avian Dis. 1993, 37: 961-969)). Thus, the inherently poor replication property of lentogenic NDV in most *in vitro* and *in vivo* conditions is well known in the art, and is often contrasted with the replication property of other pathogenic NDV strains, which does not require specific replication conditions, such as the presence of Mg^{2+} and DEAE or trypsin.

As recognized by the Federal Circuit, existing scientific knowledge relevant to the invention must be considered. (*See Capon v. Eshhar* (Case No. 03-1480, Fed. Cir.), involving an appeal of a patent interference, in which the Federal Circuit determined that the Board of Patent Appeals and Interferences erred in invalidating the claims at issue on the grounds of inadequate written description and stated that the Board should have considered existing scientific knowledge for the inventions. *See also Hybritech Inc. v. Monoclonal Antibodies Inc.*, 802F.2d 1367, 1384 (Fed. Cir. 1986), in which the court stated that "a patent need not teach, and preferably omits, what is well known in the art").

Thus, since lentogenic NDV was well known in the art as an inherently replication-deficient or replication-defective virus at the time the application was filed, the recitation of "replication-deficient NDV" does not constitute new matter.

The Examiner also states that "the HUJ strain disclosed on page 26 is not replication deficient because the virus still replicates in media without trypsin just not as efficiently as in culture with trypsin" (Office Action, at p. 6). The replication data on page 26, however, shows a very significant difference between replication with ($10^{8.5}$) and without trypsin ($10^{2.6}$ and $10^{3.0}$), and therefore further demonstrates the replication-deficient property of lentogenic NDV.

Regarding claim 27 and the claims depending therefrom, the Examiner states that the recitation "composition comprises a lentogenic oncolytic strain of NDV" is not supported by the specification as originally filed. Since claim 27 is herein cancelled, this rejection is moot. Dependent claim 28, which previous depended from claim 27, is amended to depend from claim 24.

Claims 46 and 50 remain rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement for the reasons stated on pages 6-9 of the Office Action. Applicants respectfully disagree, and note that the term "protein analog" is explicitly defined in the specification (*see* p. 8, lines 10-15). Thus, Applicants submit that it is within the knowledge of a skilled artisan to produce a protein analog without undue experimentation. In order to expedite prosecution of this application, however, claims 46 and 50 are amended to delete the recitation of "an analog or subunit thereof." Withdrawn claims 55 and 57 are similarly amended. Accordingly, this rejection should be withdrawn.

Accordingly, all rejections under 35 U.S.C. §112, first paragraph, for written description should be withdrawn.

Claims 4, 5 and 28-30 remain rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. Applicants wish to note that a deposit of HUJ is being made in the European Collection of Cell Cultures (ECACC) in United Kingdom under the terms of the Budapest Treaty. When the deposit is complete, an affidavit or declaration, or a statement by an attorney of record, will be submitted stating that the invention will be irrevocably and without restriction released to the public upon issuance of a patent. As a deposit will be made during pendency of this application, Applicants respectfully request the rejection be held in abeyance at this time until the appropriate statement can be made.

Claims 2, 3, 24-26, and 46-52 are rejected under 35 U.S.C. §102(e), as being anticipated by U.S. Publication No. US 2003/0077819 to Groene et al. ("Groene"), for the reasons stated on pages 12-14 of the Office Action. Applicants respectfully traverse.

Groene is directed to a pharmaceutical composition for treating cancer which requires a combination of an oncolytic virus and human leukocytes or human platelets. Thus, cancer in a human subject is treated by administering a pharmaceutical composition comprising human leukocytes and a replication-competent oncolytic virus. Cancer treatment according to Groene requires leukocytes for binding the virus, and the ratio of plaque-forming units of the virus to the number of leukocytes in the composition is at least 1:100. Groene further discloses treating a human subject with cancer by administering a pharmaceutical composition comprising human cells infected with an oncolytic virus, where the cells are leukocytes or platelets, thereby treating the subject.

In contrast, the pharmaceutical composition as recited in amended claim 2 consists essentially of a replication-deficient lentogenic oncolytic strain of NDV as an active ingredient, and does not include human leukocytes or human platelets. As previously explained in the Amendment filed on January 18, 2006, the composition according to the invention utilizes a replication-deficient lentogenic oncolytic strain of NDV, which produces mostly non-infectious progeny in a host cell, in direct contrast to the replication-competent viruses of Groene, which produce infectious progeny in a host cell. In this regard, Applicants again note that the unexpected finding disclosed in this application that the cytopathic effect exerted by a lentogenic oncolytic strain of NDV does not require efficient viral replication or depend on the production of infectious progeny.

For example, the application discloses that adsorption of viral surface glycoproteins to tumor cells is sufficient to exert cytotoxic effect on tumor cells, with the cytotoxic effect of the surface glycoproteins on tumor cells being achieved independently of whether the surface glycoproteins are derived from lentogenic or mesogenic strains of NDV (*see* p. 30, line 17 to p. 31, line 15; Fig. 6; Table 8). These viral surface glycoproteins do not have the capability to replicate or to produce infectious progeny. Thus, the finding that isolated glycoproteins exert cytopathic effect in tumor cells further supports the conclusion that the cytopathic effect exerted by HUJ does not require efficient viral replication, in direct contrast to the disclosure of Groene, which explicitly requires viral replication in order to induce the cytopathic effect.

Groene, therefore, does not anticipate claim 2. Groene also does not anticipate claims 3 and 24-26, which depend from claim 2, both because of their dependency from that claim as well as their inclusion of additional recitations. Claim 46 is amended to depend from allowable claim

1. Thus, claims 46-52, which depend from claim 1, directly or indirectly, are also allowable as noted above. Accordingly, Applicants respectfully request the rejection under 35 U.S.C. § 102(e) be withdrawn.

In view of the above, the entire application is believed to be in condition for allowance, early notification of such would be appreciated. In particular, the method claims should be rejoined once the composition claims are allowed since those method claims depend from and include the features of the allowable composition claims. Should the Examiner not agree that all claims are allowable, then a personal or telephonic interview is respectfully requested to discuss any remaining issues in order to expedite the eventual allowance of the claims.

Respectfully submitted,

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